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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/741,664	12/21/2000	Ayoub Rashtchian	IVGN 152.3 CON	7736

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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
08/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/741,664	RASHTCHIAN ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/29/2008 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection of claim 60 under 35 USC 112/first paragraph is moot in view of the amendments to the claim.

Claim Rejections - 35 USC § 103

4. Claim 60 is rejected under 35 USC 103(a) as being unpatentable over Holmes (WO 95/00664) in view of Gelfand (US Patent 5,618,703), Hoeltke (US Patent 5,814,502), and Scalice (US Patent 5,338,671) and Sharkey (Sharkey et al; Biotechnology, vol 12, pages 506-509; 1994).

Holmes teaches methods of performing multiple PCR reactions using different primer pair and templates to identify primer pairs suitable for detection of Salmonella species in samples (see para bridging pages 2-3; page 7, first full para; page 14, last para). Holmes teaches that the PCR reactions contained 105 uL comprising template DNA, 50mMKCL, 2.5 mM $MgCl_2$ (instant claim 26), 10 mM Tris, 200uM each dNTP (instant claim 28), 0.5% Tween, and 2.5 units of Taq

polymerase (23.8 U/ml). Holmes is silent with regard to the steps of making of the composition prior to template addition. Holmes does not teach storage of the composition at a range of -20°C to +4°C, or a PCR reaction mix containing an antibody that binds to the thermostable enzyme.

However, it was well known to those of ordinary skill in the art at the time the invention was made, that a master mix is typically employed when performing multiple reactions in order to improve efficiency and consistency and to avoid pipetting error. For example, Gelfand teaches methods of performing multiple reverse transcription reactions wherein reagents, except nucleic acid molecules, are added in a master mix containing a thermostable polymerase, such as Taq, a nonionic detergent, all 4 dNTPs, and a buffer salt (see cols 27, lines 55-65; col 30 and col 31, lines 18-40). With regard to step (b) of claim 60, Gelfand specifically teaches a method wherein multiple samples were analyzed and "for consistency and to avoid pipetting errors" the mix was prepared as a master mix and aliquoted as 17 uL into different reaction tubes such that only a single uL of primer and 2 uL of template were added (see col. 31, lines 30-40) (therefore, the composition was not diluted more than 2x upon the addition of nucleic acid molecules). Further, Hoeltke specifically teaches making compositions containing pre-mixed reaction components in liquid form so that the user only has to add an aliquot of DNA in one single pipetting step (see col. 2, lines 20-22). Hoeltke teaches a composition which comprises a DNA polymerase, such as Taq, a buffering substance, a salt, and nucleoside triphosphates (see col 2,l ines 32-50). Hoeltke teaches that these compositions exhibit particularly high stability when stored between –20 and 4 deg C. Scalice teaches that the use of an antibody specific for a thermostable DNA polymerase, such as Taq (cols 7-8), can be used to reduce or eliminate the formation of non specific products in PCR methods (see abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the multiple PCR methods using different primers and template of Holmes with the use of a master mix, stored at a temperature between -20°C to +4°C, containing all reagents necessary for the reaction such that the methods could be performed requiring only contacting the PCR master mix with nucleic acid template and primers, as taught by Gelfand and Hoeltke. The ordinary artisan would have been motivated to provide a master mix for the purpose of improving the consistency and to reduce pipetting errors in the reactions of Holmes, as taught by Gelfand. The ordinary artisan would have been motivated to store such compositions at a temperature between -20°C to +4°C because Hoeltke teaches that such compositions exhibit particular high stability when stored between -20°C to +4°C. In performing the improved methods of Holmes in view of Gelfand and Hoeltke, it would have been further prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a composition that further included at least one antibody that binds said thermostable polymerase in view of the teachings of Scalice . The ordinary artisan would have been motivated to add an antibody specific for Taq polymerase to the PCR master mix of Holmes in view of Gelfand and Hoeltke for the purpose of reducing the formation of non specific PCR products in the methods of Holmes because Scalice teaches that such antibody can be used to reduce or eliminate the formation of non specific products in PCR methods. The ordinary artisan would have been motivated to add the antibody to the PCR master mixture of Holmes in view of Gelfand and Hoeltke for the purpose of providing necessary reagents in premixed form for use in any PCR reaction.

Holmes in view of Gelfand, Hoeltke and Scalice do not teach a method where the polymerase to antibody concentration ratio is between 1:1 to 1:10, however Sharkey teaches the use of antibodies in PCR reactions to minimize non specific product formation and teaches that there is a broad optimum range of antibody concentration for effective triggering (page 508, col. 1, 3rd fill para). Sharkey exemplifies the use of different antibodies at varying concentrations from 1:1 to 1000:1 antibody to polymerase concentration ratios (see figure 1, figure 4) as well as teaching that certain antibodies were triggers when used at levels to effect 60% inhibition, including at ratios of less than 10:1 antibody to polymerase concentration ratios (see page 508, col. 1, 2nd full para and figure 1). Sharkey also teaches that TP15 was a potent inhibitor of Taq at only 6 fold molar excess. Further, as set forth in the MPEP 2144.05 II A, "Optimization of Ranges":

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.)...

Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to arrive at an optimal polymerase to antibody ratio, including the claimed recitation of 1.1 to 1:10, in the method of Holmes, Gelfand, Hoeltke, and Scalice, as taught by Sharkey. The ordinary artisan would have been motivated use the minimal amount of reagent to achieve the desired affect. It is noted that the specification provides no indication that the claimed ratio is critical, but rather provides a laundry list of possible antibody to polymerase concentration ratios varying from about 100:1 to about 1:1 (see page 13, lines 22-28.

Conclusion

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday, Wednesday and Thursday from 9:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Jehanne Sitton/
Primary Examiner
Art Unit 1634